In This Issue . . .

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Cell Surface Receptors and Psoriasis

For years, says Jonathan Mansbridge of the Psoriasis Research Institute in Stanford, California, there has been a "long and confused literature" discussing whether the neutrophils of psoriasis patients are the same as or different from those of people without psoriasis. In this issue, Wieslaw Glinski, Todd Anhalt, and Mansbridge, of Stanford University and the Psoriasis Research Institute, report on a series of experiments designed to see whether certain cell surface receptors are different on neutrophils of psoriasis patients. They report that these receptors do behave differently, but the difference is not what they expected.

The Stanford group started with a well-established observation: neutrophils contain receptors on their surface for a hexapeptide, N-formyl-Met-Leu-Phe, which is an analog of a portion of a specific bacterial protein. Presumably, these receptors enable the neutrophils to recognize bacteria and move toward them (chemotaxsis).

If there are no bacteria around, the neutrophils have only a small number of the peptide receptors on their surfaces, but in the presence of bacteria or of the bacterial peptide, the cells produce a large number of the receptors on their surfaces. Then the receptors bind to the peptide and both receptor and peptide enter the cell. Finally, the receptors that entered the cell re-appear on the cell surface as unoccupied receptors that can now find more peptide.

If investigators add a low concentration of the peptide, the number of receptors on the cell surfaces increases—a process called up-regulation. If they add a large amount of peptide, many of the receptors are tied up taking the peptide into the cells and the net number of receptors on the cell surface decreases—a process called down-regulation. Finally, researchers can block down-regulation with cytochalasin B, which interferes with the cytoskeleton of the cell.

With this armamentarium, the Stanford researchers proceeded to ask whether the neutrophils of psoriatic patients are different from normal. In psoriasis, says Mansbridge, "the one clear fact is that there are infiltrates of neutrophils into the skin." It has been proposed that these neutrophils are unusually sensitive to chemotactic substances, which might mean that the cells are more able to up-regulate their receptors.

But Glinski, Anhalt, and Mansbridge found that the neutrophils of psoriasis patients are less able to up-regulate. When the cells were exposed to just the bacterial peptide or when they were also exposed to cytochalasin B, they had fewer receptors on their surface.

It is not entirely clear why this should be the case. One possible explanation is that the cells of psoriatic patients are habituated or "desanitized" by the constant presence of chemotactic factors. This, Mansbridge points out, is pure speculation, however, and for now, all the group can say for sure is that the neutrophils of psoriatic patients are different from those of normal controls.

Treating Melanoma Without Surgery

Heat, delivered superficially to mice with melanomas, is a highly effective treatment, reports Norman Levine of the University of Arizona Health Sciences Center in Tucson. Levine, who says his goal is to use heat to treat human melanoma, reports his results in this issue.

Levine was led to the experiments with mice when he considered the effectiveness of a device, invented 10 years ago at Los Alamos National Laboratory, that can deliver radiofrequency heat. The device is "so small that you can hold it in the palm of your hand and it weighs about a pound," Levine says. For this reason, it is "very convenient in an outpatient setting."

The device is already being used to treat "cancer eye", a low-grade squamous cell cancer of cattle. Veterinarians take the device to the field where the cattle graze and use it to apply heat to the cancerous eyes. The heat treatment destroys the cancer.

So Levine, who says he is "interested, in a general way, in nonsurgical treatments for skin cancer," decided to use the device in a mouse model of melanoma. It is already well known that malignant cells are more sensitive to heat than normal cells and a number of researchers have tried to treat tumors by applying heat. But, says Levine, "nearly all hyperthermia has been delivered to deep tumors. That means you can't heat the tumors very much." Researchers typically heat the deep tumors to at most one to two degrees above body temperature—to temperatures that are generally no higher than 43 degrees. However, Levine notes, "you can deliver much higher temperatures to the skin."

Levine therefore implanted melanomas in mice to see if he could eradicate them with heat treatments and to see what, if any, are the side effects of this treatment. He finds that the melanoma is exquisitely sensitive to heat. After 30 seconds of heat treatment, there is, he says, "a remarkable clearing of the tumor with minimal effects to surrounding normal tissue." He also found that he needed to heat the tumor to at least 48 degrees, which is a much higher temperature than is typically achieved when internal tumors are heated. Now Levine is experimenting with different regimens—trying lower temperatures but repeated treatments, for example, and testing other reagents, such as topical retinoids, in addition to heat. So far, his results are very promising.